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| 09/980,954 | 02/15/2002 | Akira Kaji | K0448/7012 | 3440 |

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| EXAMINER |
|---|
| STEADMAN, DAVID J |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1656 | |

DATE MAILED: 09/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/980,954 | KAJI ET AL. | |
| | Examiner | Art Unit | |
| | David J. Steadman | 1656 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 June 2006 and 05 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 and 52-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 52-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Application*

**[1]** A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/5/2006 has been entered.

**[2]** Claims 1 and 52-59 are pending in the application.

**[3]** Applicant's amendment to the claims, filed on 6/8/2006, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

**[4]** Applicant's arguments filed on 6/8/2006 have been fully considered and are deemed to be persuasive to overcome at least one of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

**[5]** The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.

### *Sequence Compliance*

**[6]** This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37

CFR 1.821 through 1.825; applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in compliance, applicants should identify nucleotide sequences of at least 10 nucleotides and amino acid sequences of at least 4 amino acids in the specification by a proper sequence identifier, i.e., "SEQ ID NO:" (see MPEP 2422.01). If these sequences have not been listed in the computer readable form and paper copy of the sequence listing, applicant must provide an initial computer readable form (CRF) copy of the "Sequence Listing", an initial paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). See particularly the disclosed Table 8 at pp. 64-129 of the specification containing a list of atomic coordinates representing the disclosure of an amino acid sequence. Applicant should identify this sequence by a proper sequence identifier.

***Claim Rejections - 35 USC § 112, First Paragraph***

**[7]** Claims 1 and 52-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a method for using a 3-D structure of a protein "produced by a computer using" the data of Table 8 and optionally contacting the RRF protein with a compound. MPEP 2111.01 states, "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." In this case, the genus of 3-D structures produced by a computer using the data of Table 8 has been interpreted as encompassing homology models, which is supported by the specification's disclosure that "[b]y use of the structure coordinates of RRF of the present invention and by use of molecular substitution, the structure coordinates of a mutant, homologue, or co-complex or different crystal structure of RRF can be determined" (specification, p. 19, middle).

The Court of Appeals for the Federal Circuit has held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial

variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single species of the genus of 3-D structures as encompassed by the claims, *i.e.*, the 3-D structure of RRF having the structural coordinates of Table 8 and only a single species of RRF proteins, *i.e.*, SEQ ID NO:1. The specification fails to disclose any other species of 3-D structures of RRF proteins as encompassed by the genus, which encompasses species having widely variant structures and functions. The structures of the genus are widely variant in view of the specification, which, as noted above, states, "mutant, homologue, or co-complex or different crystal structure of RRF" can be used in the claimed invention (specification at p. 19, middle). The "functions" of the genus of 3-D structures and proteins are widely variant, particularly in view of the specification's definition of "RRF protein," which is "an RRF protein having an enzyme activity in an ordinary state" (p. 13, middle).

Given the lack of description of a representative number of polynucleotides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

**[8]** Claims 1 and 52-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for using the 3-D structure of RRF having the structural coordinates of Table 8 and the RRF protein of SEQ ID NO:1, does not reasonably provide enablement for a method for using a 3-D structure of a protein

"produced by a computer using" the data of Table 8 and any RRF mutant, homologue, or co-complex as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation is required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). MPEP 2164.04 states, "[w]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." Accordingly, the Factors most relevant to the instant rejection are addressed in detail below.

*The breadth of the claims*: The claims are so broad as to encompass a method for using all 3-D structures of a protein "produced by a computer using" the data of Table 8 and optionally contacting the RRF protein with a compound. MPEP 2111.01 states, "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." In this case, the genus of 3-D structures produced by a computer using the data of Table 8 has been interpreted as encompassing homology models, which is supported by the specification's disclosure that "[b]y use of the structure coordinates of RRF of the present invention and by use of molecular substitution, the structure coordinates of a mutant, homologue, or co-complex or different crystal structure of RRF can be determined" (specification, p. 19, middle). Also, the RRF proteins of claims 57-59 have been interpreted as encompassing mutants, homologues, and co-complexes of RRF proteins. The scope of the claims is not commensurate in scope with the enablement provided by the specification, particularly with respect to the recited 3-D structures and RRF proteins. In this case, the specification is enabling only for a method for using the 3-D structure of RRF having the structural coordinates of Table 8 and the RRF protein of SEQ ID NO:1.

*The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art*: At the time of the invention, methods of using a 3-D structure of a polypeptide and generating homology models were known in the prior art. However, while methods of generating homology models of a protein using a set of structure coordinates was known, Lambert et al. (US Patent Application Publication 2004/013751) acknowledges that "[p]otential or existent homology models cannot provide the necessary degree of

specificity" in the in silico design of modulators (p. 3, ¶[0017]). Further, it was well-known in the prior art that polypeptides having disparate functions could share similar 3-D structures. For example, Hegyi et al. [*J Mol Biol* (1999) 288:147-164] teaches that an isomerase, an oxidoreductase, a hydrolase, and a lyase all share the same TIM-barrel fold (p. 148, left column, and Figure 1). Similarly, while methods of altering the amino acid sequence of a protein were known at the time of the invention, the effects of such alteration(s) were highly unpredictable. Thus, a skilled artisan would have recognized that there was a high level of unpredictability in using altered 3-D protein structures and altered proteins themselves as encompassed by the claims with an expectation that the altered 3-D structures and proteins represent a biologically relevant conformation of RRF.

*The amount of direction provided by the inventor and The existence of working examples*: The specification discloses only a single working example of a 3-D protein structure, *i.e.,* a 3-D structure of RRF having the structure coordinates of Table 8 and only a single working example of an RRF protein, *i.e.,* the RRF protein of SEQ ID NO:1. The specification fails to disclose any other 3-D structures of RRF protein variants as encompassed by the claims. Further, the specification fails to provide guidance for using those variant 3-D structures of RRF that are not biologically relevant. Similarly, the specification fails to disclose any other RRF protein variants as encompassed by the claims and further fails to provide guidance for using those variant RRF proteins that are not biologically relevant.

*The quantity of experimentation needed to make or use the invention based on the content of the disclosure*: While methods of altering a 3-D structure of a protein *in silico* were known at the time of the invention, it was not routine in the art to create a substantial number of altered 3-D structures as encompassed by the claims without guidance of which of those structures is useful according to the disclosed utility. Similar reasoning applies to the RRF protein variants encompassed by the claims.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

RESPONSE TO ARGUMENT: Applicant argues the specification identifies residues of the RRF active site, which would enable a skilled artisan to practice the full scope of the claimed invention without requiring undue experimentation.

Applicant's argument is not found persuasive. The amendment to the claims to limit the method to designing or selecting compounds that bind to the *active site* of RRF is acknowledged. However, it is noted that, while the specification identifies active site residues of the RRF having the structural coordinates of Table 8, the claims are not so limited and broadly encompass designing or selecting compounds that bind to the active site of any mutant, homologue, co-complex, or different crystal structure of RRF, which, for reasons noted above, would require undue experimentation.

***Claim Rejections - 35 USC § 103***

**[9]** Claim(s) 1 and 52-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al. (US Patent 5,856,116; cited in the IDS filed 2/18/2005) in view of Kaji et al. (*Biochem Biophys Res Comm* 250:1-4, 1998) and In re Gulack 217 USPQ 401 (Fed. Cir. 1983). See MPEP §§ 2144 and 2144.04 regarding legal precedent as a source of rationale for rejection under 35 U.S.C. § 103 and see MPEP §§ 2106.IV.B.1.(b) and 2106.VI regarding determination of whether descriptive material is functional or non-functional.

Claims 1 and 52-59 are drawn to a method for identifying a compound capable of binding to RRF using a three-dimensional structure of RRF "produced by a computer using atomic coordinates of RRF protein according to Table 8" and optionally including the steps of synthesizing the compound and contacting the compound with RRF protein.

The reference of Wilson et al. teaches methods of designing and selecting compounds that bind to an enzyme using a three-dimensional model of said enzyme

(columns 9-13 and claim 1). Wilson et al. teaches that the compound can be designed de novo or by using the structure of a known compound capable of binding to the enzyme (column 12, top and claims 2 and 3). Wilson et al. teaches steps for determining the bioactivity of the compound, e.g., synthesizing the compound and determining its effect on the enzyme (claim 1, steps c and d). The method as taught by Wilson et al. is the claimed method, only missing the specific structural coordinates as disclosed in Table 8.

The reference of Kaji et al. teaches a method for assaying the activity of RRF (p. 1, right column, bottom to p. 2, left column) and further teach that RRF is a target for antibacterial agents and suggests the use of rational drug design against RRF (p. 3, right column).

In Gulack, the court held that nonfunctional descriptive material in a claim does not distinguish the prior art in terms of patentability. The key factor in analyzing the obviousness of these claims over the prior art is the determination that the computer algorithm used to identify compounds that may bind RRF is a known algorithm and is unmodified. If the difference between the prior art and the claimed invention as a whole is limited to descriptive material stored on or employed by a machine, it is necessary to determine whether the descriptive material is functional descriptive material or nonfunctional descriptive material. In this case, the RRF structural coordinates as disclosed in Table 8 are non-functional descriptive material and the method uses a known unmodified computer algorithm. Data, which are fed into a known algorithm whose purpose is to compare or modify those data using a series of processing steps,

do not impose a change in the processing steps and are thus nonfunctional descriptive material. A method of using a known comparator for its known purpose to compare data sets does not become nonobvious merely because new data becomes available for analysis. Nonfunctional descriptive material cannot render nonobvious an invention that would have otherwise been obvious.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to perform rational drug design as taught by Wilson et al. to identify a compound that binds to RRF and optionally including the steps of synthesizing the compound and contacting the compound with RRF protein, wherein only non-functional descriptive material is additionally present in the claims, which do not distinguish the claimed methods from those taught by Wilson et al. and Kaji et al. according to In re Gulack. One of ordinary skill in the art would have been motivated to practice the method of Wilson et al. in view of the teachings of Kaji et al. One of ordinary skill in the art would have had a reasonable expectation of success for practicing the claimed method because of the teachings of Wilson et al. and Kaji et al. Therefore, claims 1 and 52-59 would have been obvious to one of ordinary skill in the art at the time of the invention.

RESPONSE TO ARGUMENT: Applicant argues the amendment to require that the structural coordinates are processed by a computer obviates the rejection in view of the Court's holding in *In re Lowry* 32 USPQ2d 1031 (Fed. Cir. 1994) that "[t]he printed matter cases have no factual relevance where 'the invention as defined by the claims

requires that the information processed by the mind but by a machine, the computer.'" According to applicant, the Trilateral Report should not sustain the rejection in view of the claim amendment.

Applicant's argument is not found persuasive. Contrary to Applicant's assertion, the situation in *Lowry* is not analogous to the instant case – even in view of the amendment to require that the 3-D structure is produced by a computer. The case in *In re Lowry* involved a claim to a "memory for storing data" comprising a series of attribute data objects (ADOs). The *Lowry* Court held that "ADOs contain both information used by application programs and information regarding their physical interrelationships within a memory." Lowry's data structures were held to "impose a physical organization of the data," which "increased computing efficiency." As such, the Court held that "Lowry's ADOs do not represent merely underlying data in a database." In other words, because Lowry's ADOs were *functionally interrelated* with the memory of the computer to increase computing efficiency, the data were not held to be merely non-functional descriptive material. As such, the Court held that the printed matter cases do not apply. In contrast to *Lowry*, the data of Table 8 have no such functional relationship with the computer that processes the data. In this case, there is no evidence of record that the data of Table 8 functionally affect the processing steps of the computer. For example, there is no evidence that the data of Table 8 interact with other computer hardware or software to affect the efficiency or accuracy or any other characteristic of computer processing. Rather the data of Table 8 appear to be used merely as input for a computer program that generates a three-dimensional structure of an RRF polypeptide.

In other words, the data recited in claim 1 do not affect how a computer performs or functions. The examiner's position that the data of Table 8 is non-functional descriptive material is further supported by MPEP 2106.VI, which provides "[c]ommon situations" that involve nonfunctional descriptive material, including "a computer-readable storage medium that differs from the prior art solely with respect to nonfunctional descriptive material, such as music or a literary work, encoded on the medium," "a computer that differs from the prior art solely with respect to nonfunctional descriptive material that cannot alter how the machine functions (i.e., the descriptive material does not reconfigure the computer)," and "a process that differs from the prior art only with respect to nonfunctional descriptive material that cannot alter how the process steps are to be performed to achieve the utility of the invention." These "common situations" are analogous to the instantly claimed method that differs from the prior art method solely with respect to the non-functional descriptive material of Table 8. According to MPEP 2106.VI, "[n]onfunctional descriptive material cannot render nonobvious an invention that would have otherwise been obvious." Accordingly, because the only difference between the method as taught by the combination of prior art references and the claimed method is limited to the data of Table 8, the method of claims 1 and 52-59 would have been obvious to one of ordinary skill in the art at the time of the invention.

***Conclusion***

**[10]** Status of the claims:

Claims 1 and 52-59 are pending.

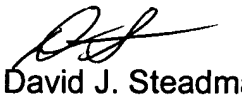
Claims 1 and 52-59 are rejected.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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